IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
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A.E. COLVIN, Jr.	)	
	)	
Serial No. 09/920,627	)	Examiner: M. Cole
	)	
Filed: August 3, 2001	)	Group Art Unit: 1743
	)	

For: DETECTION OF ANALYTES IN AQUEOUS ENVIRONMENTS

RESPONSE

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This is in response to the Office Action mailed May 6, 2003.

At the outset, Applicant acknowledges with appreciation the indication of allowability of claims 5, 8, 9, 13, 18, 21, 22, 26, 31, 34, 35, 39, 45, 52 and 57. However, in the August 2, 2002 Action, claims 47, 54 and 59 were indicated to be allowable, yet claims 47 and 54 are subject to the pending rejection under 35 USC §102(e), and claim 59 is neither rejected nor indicated to be allowable in the present Action. Given the clear indication of allowability in the prior Action, and the lack of any reason given in the present Action for the withdrawal of the indication of

allowability, and the apparent failure to follow the procedure set forth in MPEP §706.04, it is assumed that claims 47, 54 and 59 should have been included in the list of allowable claims. If that is not the case, clarification is respectfully requested.

35 USC §102

Reconsideration and withdrawal of the rejection of claims 1-4, 6-7, 10-12, 14-17, 19-20, 23-25, 27-30, 32-33, 36-38, 40-44, 46-51, 53-56 and 58 under 35 USC §102(e) as being anticipated by Van Antwerp '954 are respectfully requested.

As noted above, claims 47 and 54 were previously indicated to be allowable, and are now subject to this rejection. Moreover, claims 6-7, 19-20, 32-33, 40, 46 and 53, which were previously rejected on different grounds (now withdrawn), are now rejected for the first time as anticipated by Van Antwerp '954. In view of that, it is respectfully submitted that the finality of the present Action is premature. MPEP §706.07(a) states that:

> Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

The rejection of claims 6-7, 19-20, 32-33, 40, 46 and 53 as anticipated by Van Antwerp '954 is a new ground of rejection. Moreover, it was neither necessitated by applicant's amendment (none of those claims has been amended) nor based on information submitted in an information disclosure statement (no IDS was filed subsequent to the last amendment). The finality is premature and should be withdrawn.

Turning to the substance of the rejection, in each instance, the claimed indicator macromolecule is a copolymer of a) one or more indicator component monomers, which individually are not sufficiently water soluble to permit their use in an aqueous environment, and b) one or more hydrophilic monomers. In other words, the indicator component monomer is an integral part of the polymer.

In contrast, Van Antwerp '954 does not disclose or suggest any such copolymers. Van Antwerp '954 is directed to an implantable amplification system which includes an amplification component immobilized in a polymer matrix. The immobilization takes place "either by entrapment or by covalent attachment" (col. 3, lines 32-35). The Van Antwerp '954 patent uniformly describes the relationship between the amplification components and the polymer matrix

as two separate entities in which the former is entrapped within or covalently attached to the latter. See, *e.g.*, col. 3, lines 32-35; col. 7, line 60 to col. 8, line 4; col. 10, lines 25-28; col. 11, lines 7-10; and col. 15, lines 11-15. The following is illustrative:

> In the present invention, the transduction system, or signal amplification components are entrapped within a suitable polymer matrix. Alternatively, the amplification components can be covalently attached to, and surrounded by the polymer matrix. Covalent attachment of the components to a polymer matrix prevents leakage of the components to surrounding tissue, and other undesirable contact of the amplification components with non-target fluids.

Col. 7, line 63 to col. 8, line 4. Thus, Van Antwerp '954 lacks any disclosure or suggestion of copolymerizing one or more indicator component monomers with one or more hydrophilic monomers to form an indicator macromolecule, and for that reason cannot anticipate any of the rejected claims.

The Action contends (page 3) that the Van Antwerp '954 indicator can be bound to the polymer as presently claimed, but no support is advanced for that contention; indeed, it is contrary to the record. There is a big difference between copolymerizing two (or more) monomers to form a copolymer of which the indicator component monomer is an integral part (as presently claimed), and covalently attaching an indicator to an already-formed polymer (as

disclosed in Van Antwerp '954). As a consequence of the present claims, the backbone of the copolymer includes structures corresponding to both the hydrophilic monomer and the indicator monomer. Van Antwerp '954's backbone, in contrast, contains at most only the hydrophilic polymer, with the indicator molecules being pendant therefrom like charms hanging from a bracelet. This may be depicted schematically as follows:

$-(H)_m-(I)_n-(H)_m-(I)_n-$ *vs.*

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-H-H-H-H-H-H-H-
 |   |   |
 I   I   I
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Present claims Van Antwerp '954

where H indicates a hydrophilic monomer residue, I indicates the indicator residue, and m and n relate to the relative concentrations of H and I. Those are fundamentally different structures. It would be readily apparent that the structure resulting from the present claims would be more stable than that of Van Antwerp '954, because in the present case the indicator is an integral part of the polymer, whereas in Van Antwerp '954, the indicator is either covalently attached to the preexisting polymer, or physically (non-covalently) entrapped within the polymer. The present copolymerization scheme also allows for the incorporation of a higher concentration of the indicator compared to the Van Antwerp '954 scheme,

resulting in improved signal strength. The claimed copolymerization is also more efficient than the Van Antwerp '954 immobilization from the perspective of needing fewer reagents. There simply is no disclosure in Van Antwerp '954 of the presently-claimed copolymerization scheme.

The presently-claimed structure also allows for the production of an excimer effect, as described on pages 14-16 of the specification. The Action alleges that the Van Antwerp '954 anthracene indicator would be capable of an excimer effect, but that is unsupported and irrelevant. It does not matter what a reference is capable of-what matters is what is disclosed by the reference. The possibility of excimer formation is not even hinted at in Van Antwerp '954, and there is no disclosure or suggestion in that reference that any of its amplification systems did in fact exhibit such an effect.

The Action supports the rejection by arguing that the present specification recognizes that anthracene can possess an excimer effect, therefor Van Antwerp '954, which supposedly uses anthracene, must have the same effect. That argument has no merit. The present specification acknowledges that anthracene and pyrene may form excimers, but it goes on to say that such occurs only at relatively

high concentrations (page 15, lines 15-22). It does *not* say that anthracene derivatives, such as those disclosed in Van Antwerp '954 or claimed in the present application, would have been expected to have that characteristic. For the reasons shown below, they would not have been expected to have that characteristic.

It is submitted that one would recognize that the excimer effect would not have been possible in Van Antwerp '954. As noted above, the excimer effect is concentration-dependent. The most pertinent disclosure in Van Antwerp '954 of the concentration of the reactants is at col. 15, lines 48-51, wherein the amount of amplification component used is in the range of about 0.5% to about 10%, based on the total weight of the matrix. In Example 2 of the present specification in which the effect is described in detail, it occurred when the molar ratio of hydrophilic monomer:indicator component monomer was about 5:1. That corresponds to approximately 50% indicator monomer by weight, based on the total weight of the copolymer. The concentration range disclosed in Van Antwerp '954 is considerably less than that used by applicant to achieve the excimer effect. It appears unlikely that an excimer effect could have been achieved at those low concentrations.

Therefore, because Van Antwerp '954 contains no disclosure at all of an excimer effect, and is very unlikely to have created one at the low concentrations that it discloses, it cannot anticipate the present claims that recite an excimer effect.

In addition, one of the great and surprising advantages of the excimer effect in applicant's claimed methods and systems is the discovery that the excimer emission region is *not* responsive to changes in analyte concentration, but *is* responsive to other aspects tested, such as excitation intensity, temperature and pH (page 16, lines 7-22). That allows macromolecules having that effect to serve as both an indicator and as an internal reference. That feature is specifically recited in rejected claims 44, 51 and 56. Van Antwerp '954 cannot possibly anticipate those claims because (in addition to not disclosing copolymers or excimers) it contains no disclosure of an indicator macromolecule serving as its own reference.

Thus, Van Antwerp '954 cannot anticipate any of the rejected claims.

As the case is believed in condition for allowance, a favorable Action is respectfully requested.

Respectfully submitted,

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